

**AN IN VIVO PROTEIN SCREEN BASED ON
ENZYME-ASSISTED CHEMICALLY INDUCED DIMERIZATION ("CID")**

Abstract of the Invention

A method for identifying which protein from a pool of candidate proteins catalyzes in a cell a bond forming reaction between a first substrate and a second substrate, comprising:

(a) providing a dimeric small molecule which comprises a known moiety that binds a known receptor domain covalently linked with a moiety that contains the first substrate;

(b) introducing the dimeric molecule into a cell which comprises

i) a first fusion protein comprising the known receptor domain,

ii) a second fusion protein comprising the second substrate,

iii) a protein from the pool of candidate proteins, and

iv) a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;

(c) permitting the dimeric molecule to bind to the first fusion protein and to enzymatically form a bond with the second fusion protein so as to activate the expression of the reporter gene;

(d) selecting which cell expresses the reporter gene; and

(e) identifying the protein that catalyzes the bond formation reaction in the cell between the first substrate and the second substrate. The method is also adapted to identify which substrate from a pool of candidate substrates is selected in a cell by a known enzyme for a bond forming reaction between the substrate and a known amino acid. Also, cells, compounds and kits for carrying out the methods.